IN THE SPECIFICATION

Please replace paragraphs [0054], [0058], [0060], [0062], [0063], [0065], [0072], [0073], [0078], [0084], [0090], [0097], [0100], [0106], [0109] on pages 10 to 22, with the following amended paragraphs:

[0054] In another embodiment, a fully functional replacement tissue is able to withstand at least the stresses and strains imposed by normal bodily activity on the type of tissue the construct is to replace.

[0058] In accordance with the most preferred embodiment of the present invention, the matrix layer 3 of the implant is composed of Type I collagen, but can be formed, and is not limited to recombinant collagen proteins as chitosan, chitin, ubiquitin, elastin, polyethylene oxide vimentin, fibronectin, and combinations thereof.

[0060] In another embodiment of the present invention there is [[to]] provided such an implant in which one of bone anchors 1 is adapted to be pulled through a tunnel in, for example, the femur to allow fusion thereto and the other bone anchor 1 portion is adapted to be pulled through a tunnel in the tibia to allow fusion thereto to provide a substitute for the natural cruciate ligament, the segment being adapted to be placed under tension between the tunnels to provide a ligament function. Similar procedures may be employed to provide connective tissue function to other bone joints.

[0062] In accordance to another preferred embodiment of the invention, the implant may be lyophilized after its preparation. This process avoids the use of chemicals to strengthen the matrix layer 3 of the implant, to allow the reinforcement of the links between the bone plugs and the collagen layer polymerized into their trabecular structure. Also, lyophylization permits the preparation of implants adding superposed matrix layers 3 to reinforce the structure of a bioengineered connective tissue, or conferring a higher resistance to rupture before and during surgical implantation procedures.

[0063] Another important embodiment of the invention is that lyophylization may allow to form matrix layers 3 onto the implant with other biomaterials, as for example, but not limited to elastin, in combination or not with collagen, and replacing the bone anchors 1 of the implant by other porous anchors 1, as for example, but not limited to cement, or ceramic.

[0065] In accordance with the present invention, there is provided a device and method for cyclic matrix stretching and mechanical testing. A cyclic traction machine is disclosed. In a preferred embodiment, the matrix is maintained in place in the cycling chamber by inserting the two bone anchors 1 in metal pins, one fixed to a load cell and the other, attached to a motion controlled cursor. By controlling the position of the cursor, the matrix is subjected to cyclic traction with stretching amplitudes from 0 to 30 mm at a frequency of up to 1 Hz for lower amplitudes, for any extended period of time. The whole system is controlled via a LABview VI software. The operator may change easily the traction conditions and supervise the ongoing tests to make sure that everything is running smoothly. A set of matrix may be maintained under static tension, or subjected to a cyclic tension. The cells in a matrix as described in the present invention, may be induced to take a structural organization when submitted to tension stimulus. The stimulus may be also simply waves in a culture medium by agitation of the petri dishes in which is kept a matrix, or an electric stimulus.

[0072] A transverse hole (1/8-in. diam.) is made in each bone anchor 1 (FIG. 2). The bone plugs are kept in 100% ethanol overnight to be sterilized. A surgical thread resorbable within 1 month post-surgery, is passed through the transverse holes of 2 bone anchors 1 and fixed between the bones by simple stitching. Then the thread is twisted between the bones to thicken the link (FIG. 3).

[0073] A longitudinal hole or more (1 mm diam. or wider) is made in each bone anchor 1. Such holes are drilled in order to increase hydrated collagen adhesion with the bones. This step is optional. The 2 sterile bone plugs readily linked by the twisted surgical thread are transferred in a sterile plastic tube and kept in position by passing a hot metal pin through their transverse holes and across the tube (FIG. 4).

[0078] The mixture is quickly poured in the sterile plastic tube containing the 2 bone anchors 1 linked by the twisted surgical thread.

[0084] A second layer of hydrated collagen is made as described in section B (no cell is included within the matrix). The acellular ACL substitute is a network of collagen fibers (FIG. 9A). After its polymerization overnight, the acellular ACL substitute is put in culture medium containing LF suspended in the medium (DME supplemented with 10% FCS, 50 .mu.g/ml ascorbic acid, 100 IU/ml penicillin G and 25 .mu.g/ml gentamicin; FIG. 11, step 8). Within 24 hrs, the cells attach and migrate into the outer hydrated collagen layer (not lyophilized; FIG. 9B). The cells contract the collagen matrix while colonizing it within 48 hrs (FIG. 9C) The bilayered cell-populated ACL substitute can be kept in culture until grafted (FIG. 11, step 9). More hydrated matrix layers 3 can be added around the bACL.

[0090] The bone anchors 1 of the graft may be fixed with screws and/or cement (including biomedical epoxy).

[0097] Holes are made in each bone anchor 1, as previously described. The 2 sterile bone plugs readily linked by the twisted surgical thread are transferred in a sterile plastic tube and kept in position by passing a hot metal pin through their transverse holes and across the tube (FIG. 4).

[0100] The mixture is quickly poured in the sterile plastic tube containing the 2 bone anchors 1 linked by the twisted surgical thread. Collagen scaffolds are casted between two bone anchors 1 described in example I. The tissue constructs are put into a dessicator under

minimal horizontal tension, under normal atmospheric pressure or less (ranging from about 25 to 0 mm Hg). [[Tha]] The appearance of the macroscopic aspect of a bioengineered ACL ready for implantation can be seen in FIG. 12, as well as immediately after implantation in situ (opened goat's knee joint) (FIG. 13). The scaffolds were completely dehydrated within about 2-3 hrs (FIG. 14). FIG. 15 shows a histological section of a collagen matrix dehydrated under these conditions.

[0106] Holes are made in each tooth, as previously described. A sterile tooth is linked to a bone anchor 1 by a twisted surgical thread and both are transferred in a sterile plastic tube and kept in position by passing a hot metal pin through their transverse holes and across the tube.

[0109] The mixture is quickly poured in the sterile plastic tube containing the bone and the tooth anchors 1 linked by the twisted surgical thread. Collagen scaffolds are casted between two anchors 1. The tissue constructs are lyophilized or put into a dessicator under minimal horizontal tension, under normal atmospheric pressure or less (ranging from about 25 to 0 mm Hg). When totally dehydrated, the scaffolds are rehydrated in fresh DMEM, taken out of the tube and then transferred into a new sterile plastic tube. Another layer of hydrated collagen can be added containing living fibroblasts, to produce larger and stronger ligament substitutes. The periodontal ligament substitute can be implanted in the gum (FIG. 17).